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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/622,846	07/10/2001	Margaret O'Brien	55043	8176
21874	7590	10/22/2003	EXAMINER	
EDWARDS & ANGELL, LLP P.O. BOX 9169 BOSTON, MA 02209			MYERS, CARLA J	
			ART UNIT	PAPER NUMBER
			1634	

DATE MAILED: 10/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/622,846	O'BRIEN ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 27-71 is/are pending in the application.
- 4a) Of the above claim(s) 44-63 and 65-71 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 27-43 and 64 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☒ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group I, methods for diagnosing susceptibility to normal or abnormal pregnancy by determining the sequence of an HLA-G nucleic acid, in the response of July 24, 2003 is acknowledged. It is noted that the methods of group I and IV have been rejoined. Additionally, the requirement for an election of a specific polymorphism has been withdrawn. Applicants election of the nucleic acid of SEQ ID NO: 18 is acknowledged. The claims of group I are presently generically drawn to methods for detecting HLA-G nucleic acids and do not require the use of a primer or probe consisting of a particular nucleic acid sequence. Accordingly, the requirement to elect a specific nucleic acid sequence is moot as it applies to the present claims. If the method claims are amended to recite specific nucleic acid sequences, then the restriction requirement for a single nucleic acid sequence will be re-instated. As amended, the claims which correspond to group I and which have been examined herein consist of claims 27-43 and 64. Claims 66-71 are withdrawn from consideration as being drawn to a non-elected invention (group VI as set forth in the Office action of 9/23/02). Additionally, claims 44-63 and 65 and the subject matter in claims 27-43 and 64 constituting the inventions of groups II, III and V-X is withdrawn from consideration. Claims 27-43 and 64 have been examined only to the extent that they read on methods of diagnosing a condition by directly assaying the sequence or quantity of HLA-G nucleic acids.

Applicants traversed the restriction requirements on the ground(s) that the special technical feature linking the claimed inventions is "the use of the polymorphisms of the HLA-G in diagnosis." However, the technical feature linking the inventions to methods and kits is actually the HLA-G polymorphisms themselves. The codon 93 polymorphism and the 14 bp deletion in exon 8 were known in the art at the time the invention was made, as set forth on page 3 of the specification. Since the technical feature linking the claimed inventions was known in the art, there is no special technical feature linking the recited groups, as would be necessary to fulfill the requirement for unity of invention. Further, where multiple methods are claimed, the first method is considered to be the main invention and any subsequently recited methods are not considered to share a special technical feature with the main invention or any such other invention. See 37 CFR 1.475(d). Thereby, the claimed methods for analyzing HLA-G proteins and the biological activity of these proteins constitute additional methods, which require different process steps and utilize different reagents. Additionally, the methods do not share a special technical feature that is a contribution over the art.

The requirement is still deemed proper and is therefore made FINAL.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Ireland as 980134 (as set forth in the Oath). It is noted, however, that applicant has not filed a certified copy of the 980134 application as required by 35 U.S.C. 119(b). This 371 application was filed with a foreign priority document from

Ireland of 990107. The 990107 includes a stamp for PCT/IE00012 and is marked "True COPY AS LODGED." While a copy of the document 980668 has been received by the Office, a copy of the 980134 document has not been received.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-43 and 64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for diagnosing an increased risk of susceptibility to pre-eclampsia or miscarriages in a human subject wherein said methods comprise analyzing the HLA-G nucleic acids of maternal and paternal subjects for the presence of a polymorphism at position 1488 of the HLA-G gene or for the I/D-E8 polymorphism in the HLA-G wherein if a maternal subject is homozygous for the 1488T allele and for the I-E8 allele or if the paternal subject has the 1488C/D-E8 allele and 1488T/I-E8 allele, there is an increased risk for pre-eclampsia or recurrent miscarriage, does not reasonably provide enablement for methods which diagnose susceptibility to normal pregnancy, intrauterine growth retardation or miscarriage related infertility or for methods which diagnose to normal pregnancy, pre-eclampsia, eclampsia, intrauterine growth retardation, miscarriage and miscarriage-related infertility by detecting any polymorphism in the HLA-G gene or any polymorphism linked to a HLA-G polymorphism that is associated with normal pregnancy, pre-eclampsia, eclampsia, intrauterine growth retardation, miscarriage and miscarriage-related

infertility. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in formulating this rejection (*In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Case law has established that “(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without ‘undue experimentation.’” *In re Wright* 990 F.2d 1557, 1561. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that “(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art”. The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that “(l)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement”. In the instant case, the state of the art of diagnosing normal pregnancy, pre-eclampsia, eclampsia, intrauterine growth retardation, miscarriage and miscarriage-related infertility is highly unpredictable as are methods for identifying

polymorphisms in a gene or linked to a gene or polymorphism associated with of normal pregnancy, pre-eclampsia, eclampsia, intrauterine growth retardation, miscarriage and miscarriage-related infertility and the specification has not provided sufficient guidance to enable the skilled artisan to practice the method as it is broadly claimed for the following reasons:

The claims are broadly drawn to methods for diagnosing normal pregnancy, pre-eclampsia, eclampsia, intrauterine growth retardation, miscarriage and miscarriage-related infertility wherein said methods comprise detecting at least one HLA-G or HLA-G linked polymorphism in a male, female or fetus and comparing the polymorphism to a HLA-G or HLA-G linked polymorphism associated with normal pregnancy, pre-eclampsia, eclampsia, intrauterine growth retardation, miscarriage and miscarriage-related infertility wherein the presence of an HLA-G or HLA-G linked polymorphism associated with a condition selected from the group of conditions of normal pregnancy, pre-eclampsia, eclampsia, intrauterine growth retardation, miscarriage and miscarriage-related infertility is indicative of susceptibility to said condition. However, the specification teaches the identity of only 2 HLA-G polymorphisms that are associated with the occurrence of pre-eclampsia and miscarriage, namely a mutation at nucleotide position 1488 of the HLA-G gene (C/T 1488) and a 14 bp deletion in exon 8 of the HLA-G gene. The specification does not teach any additional polymorphisms associated with the stated diseases. It would require undue experimentation for one of skill in the art to screen the HLA-G gene and any gene from the human genome that might be linked to the HLA-G gene or a polymorphism therein for additional polymorphisms and then

determine which of the multitude of polymorphisms are associated with and can be used to diagnose disease. While techniques are known in the art for sequencing DNA and for identifying polymorphisms in general, such techniques provide only a research tool for discovering the reagents that can be used within the claimed invention. Further, assays for discriminating between inoperative and operative embodiments do not provide sufficient guidance and teachings as to the identity of specific polymorphisms which can be used in the claimed methods. The specification does not provide any examples of polymorphisms linked to the C/T 1488 or the I/D-8E polymorphisms and does not teach a representative number of polymorphisms which fall within the genus of any HLA-G or HLA-G linked polymorphism associated with a condition selected from the group of conditions of normal pregnancy, pre-eclampsia, eclampsia, intrauterine growth retardation, miscarriage and miscarriage-related infertility. For example, there are no teachings of any polymorphisms in the 5' or 3' untranslated region of HLA-G, in HLA-G introns or in exons of HLA-G other than exon 3 and 8. The unpredictability in the art of identifying a polymorphism associated with pre-eclampsia or recurrent miscarriage is supported by the teachings in the specification. As taught in the specification, the association of an allele with pre-eclampsia or recurrent miscarriage is not based solely on the presence of the allele itself in a fetus, but on the origin of that allele, such that the alleles associated with pre-eclampsia and recurrent miscarriage are distinct for the mother and father. The teachings in the specification indicate that allele transmission of HLA-G to PE offspring is distorted. Since the maternal and paternal effects are distinct, the analysis of fetal DNA must be accompanied by the analysis of at least one of the

parents in order for the results to be informative regarding susceptibility to pre-eclampsia or recurrent miscarriage. Additionally, the presence of single polymorphism alone does not appear to be sufficient for diagnostic purposes since the specification teaches that it is the combination of alleles that are associated with pre-eclampsia and recurrent miscarriage, i.e., homozygosity for the 1488T allele and for the I-E8 allele in females or the presence of a 1488C/D-E8 allele and a 1488T/I-E8 allele in male parents. The unpredictability of diagnosing pregnancy outcome by detecting HLA-G polymorphisms is further emphasized by the teachings in the art. For example, Steffensen (Human Biology, 1996, XP-002105902) teaches that there was no difference in the frequency of HLA-G alleles in control mother's and mother's having recurrent spontaneous abortions (RSA). Steffensen states that "the HLA-G PCR-RFLP type of the mother seems to be irrelevant for the pathogenesis of RSA." Humphrey studied linkage between the I/D-E8 polymorphism and pre-eclampsia and reported that there was no detectable relationship between this polymorphism and susceptibility to pre-eclampsia. Karhukorpi analyzed HLA-G alleles in Finnish couples by a PCR-RFLP method and reported that there was no detectable relationship between recurrent spontaneous miscarriage and the HLA-G locus. Yamashita analyzed exons 2, 3 and 4 and intron 4 of the HLA-G for polymorphisms in Japanese couples and reported that HLA-G polymorphisms were not associated with recurrent spontaneous abortion. Aldrich analyzed the deletion in exon 3 of the HLA-G gene (1597 Δ C) and reported this alleles is not a significant risk factor for pre-eclampsia or IUGR.

Furthermore, it is unpredictable as to whether the disclosed polymorphisms of HLA-G gene (C/T 1488) and a 14 bp deletion in exon 8 of the HLA-G gene are associated with and can be used to diagnose normal pregnancy, intrauterine growth retardation or miscarriage-related infertility. There are no teachings in the specification to support the conclusion that the C/T 1488 allele or I/D-8E allele or any other HLA-G allele is associated with normal pregnancy. Normal pregnancy includes conditions in addition to the lack of pre-eclampsia and recurrent miscarriage, such as conditions in which the mother does not experience pre-term birth or any pregnancy complications. The finding that mothers homozygous for the 1488T allele and for the I-E8 allele and fathers having the 1488C/D-E8 allele and 1488T/I-E8 alleles are more susceptible to contributing to pregnancies with an increased risk of pre-eclampsia and recurrent miscarriage does not mean that individuals who lack these haplotypes will thereby have normal pregnancies. It is also highly unpredictable as to whether the findings observed with pre-eclampsia and recurrent miscarriage could be applied to intrauterine growth retardation, miscarriage in general and miscarriage-related infertility. The specification has not established a universal relationship between the C/T 1488 and I/D-E8 alleles and all forms of abnormal pregnancy.

Lastly, the specification has not established that the disclosed polymorphisms cause a change in the level of a HLA-G mRNA or a HLA-G linked mRNA. There are no teachings in the specification to show that the disclosed polymorphisms are associated with an increase or decrease level of expression of a particular mRNA or with a change in the stability of a mRNA. The specification does not exemplify any methods wherein

an individual is diagnosed as being of increased susceptibility of having a normal pregnancy, pre-eclampsia, eclampsia, intrauterine growth retardation, miscarriage and miscarriage-related infertility wherein the diagnosis is performed by assaying for levels of mRNA. It is highly unpredictable as to whether an alteration in an HLA-G gene or an undefined HLA-G linked gene would result in a change in the expression level or stability of a mRNA. In the absence of evidence establishing an association between an polymorphism and mRNA levels, undue experimentation would be required for one of skill in the art to conduct the research required to identify polymorphisms which could be used to screen for susceptibility to normal pregnancy, pre-eclampsia, eclampsia, intrauterine growth retardation, miscarriage and miscarriage-related infertility by detecting HLA-G or HLA-G linked mRNA levels.

In view of the unpredictability in the art and the lack of specific guidance and teachings in the specification, undue experimentation would be required to practice the invention as it is broadly claimed.

4. Claims 27-43 and 64 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to methods for diagnosing a condition selected from susceptibility to normal pregnancy, pre-eclampsia, eclampsia, intrauterine growth retardation, miscarriage and miscarriage-related infertility, wherein the methods comprise detecting an HLA-G or HLA-G linked polymorphism and comparing the polymorphism to a HLA-G or HLA-G linked polymorphism associated with normal

pregnancy, pre-eclampsia, eclampsia, intrauterine growth retardation, miscarriage and miscarriage-related infertility. The specification teaches 2 polymorphisms in the HLA-G gene that are associated with pre-eclampsia, namely a C to T polymorphism at nucleotide position 1488 (corresponding to codon 93) and a 14 bp deletion in exon 8, referred to as I/D-E8. While HLA-G nucleic acids comprising a polymorphism at position 1488 or comprising the 14 bp deletion in exon 8 and methods which detect said polymorphism meet the written description requirements of 35 U.S.C. 112, first paragraph, the specification does not disclose and fully characterize the genus of any HLA-G or HLA-G linked polymorphism associated with normal pregnancy, pre-eclampsia, eclampsia, intrauterine growth retardation, miscarriage and miscarriage-related infertility. *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is now claimed”. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that “An adequate written description of a DNA...’ requires a precise definition, such as by structure, formula, chemical name, or physical properties’, not a mere wish or plan for obtaining the claimed chemical invention”. In

analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, only 2 member of the broadly claimed genus of polymorphisms have been identified by their complete structure, i.e. C1488T polymorphism and the I/D-E8 polymorphism. It is then determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g., in terms of functional activity). In the instant case, no such identifying characteristics have been provided for any additional polymorphisms. The claims include HLA-G linked polymorphisms. The claims do not characterize the degree to which the detected polymorphism is linked to a HLA-G polymorphism. Further, even if the claims were limited to polymorphisms that are in linkage disequilibrium with HLA-G polymorphisms, the specification does not describe in terms of their structure any polymorphisms that are in linkage disequilibrium with C1488T or I/D-E8 or any other HLA-G polymorphism. The broadest reasonable interpretation of the claims indicates that the claims are inclusive of a large genus of polymorphisms present at any position in the HLA-G gene, including the promoter, 3' and 5' untranslated regions, exon and intron regions of the HLA-G gene and any polymorphism from any other gene that may be linked to some degree to a HLA-G polymorphism. While one could contemplate a nucleotide substitution at each and every position in the HLA-G gene, such substitutions are not considered to be equivalent to polymorphisms associated with specific conditions. Rather, polymorphisms in the HLA-G gene and genes linked thereto associated with normal pregnancy, pre-eclampsia, eclampsia, intrauterine growth retardation, miscarriage and miscarriage-related infertility represent a distinct group of nucleotide variations which are expected to occur at only specific locations within the gene and consist of specific nucleotide alterations. Accordingly,

knowledge of the sequence of the wild-type HLA-G gene does not allow the skilled artisan to envision all of the contemplated polymorphisms encompassed by the claimed genus. As written the claims (with the exception of claim 36) do not recite any structural features for the polymorphisms to be detected. The specification does not disclose a common structural feature representative of the claimed genus of polymorphisms. For these reasons, Applicants have not provided sufficient evidence that they were in possession, at the time of filing, of the invention as it is broadly claimed and thus the written description requirement has not been satisfied for the claims as they are broadly written. Applicants attention is drawn to the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27-43 and 64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 27-43 and 64 are indefinite over the recitation of "HLA-G linked polymorphism" and "HLA-G linked nucleic acid." This phrase is not defined in the specification and there is no art recognized definition for this phrase. While it is clear in the art as to what is intended to be meant by a gene or polymorphism which is in linkage disequilibrium with another gene or polymorphism, it is not clear as to what is intended to be meant by a linked polymorphism. For example, it is unclear as to whether

the polymorphism is physically linked such that it is adjacent to or present within the HLA-G gene or if the polymorphism is genetically linked to any degree to the HLA-G gene.

Claim 32 is indefinite because it is not clear as to how the step of determining the level of the HLA-G or HLA-G linked mRNA is related back to the remainder of the claim since the claim requires detecting the presence of a HLA-G HL-A linked polymorphism and is not drawn to a method of detecting mRNA levels.

Claim 36 is indefinite over the recitation of "the HLA-G nucleic acid is analyzed for one or more of..." because it is not clear as to whether this step is performed in addition to the step of detecting the HLA-G or HLA-G linked polymorphism or whether this step is considered to further define the step of detecting the HLA-G or HLA-G linked polymorphism. It is unclear as to how the step of analyzing the stated alleles is related to the method of diagnosis.

Claims 37 and 38 are indefinite and confusing because it is not clear as to what is intended to be encompassed by the recitation of "the effect of one or more of the HLA-G sequences variants." It is unclear as to how a variant has an effect on the size or level of mRNA. Claims 37 and 38 are further indefinite because it is not clear as to how "the effect" is intended to be related to the remainder of the claim. It is unclear as to whether the claims are intended to include a process step of determining the size of the mRNA or the level of the mRNA. The recitation of "is measured" does not constitute an active process step. Further, it is unclear as to how a step of measuring the size or level

of HLA-G mRNA would be related to the remainder of the method which consists of the steps of obtaining, determining and comparing.

Claims 37 and 38 are indefinite over the recitation of "the sequence variants" because this phrase lacks proper antecedent basis. The claims are also indefinite in that they refer to the "method of claim 33-35" and thereby depend from multiple methods simultaneously, rather than to the methods alternatively.

Claims 39 and 40 are indefinite over the recitation of "all or part of the HLA-G sequence or HLA-G linked sequence is amplified" because the claims do not set forth how this step is intended to be related to the remainder of the method.

Claim 42 is indefinite over the recitation of "the HLA-G sequence" because this phrase lacks proper antecedent basis.

Claim 43 is indefinite over the recitation of "the nucleic acid sequence" because this phrase lacks proper antecedent basis. Additionally, it is unclear as to how this step relates back to the remainder of the claim since the claim includes the steps of obtaining, detecting and comparing but does not include a step of determining a sequence.

Claim 64 is indefinite over the recitation of "nucleic acid is measured" because the claims do not previously refer to nucleic acid per se and it is unclear as to how this step is intended to be related back to the method of diagnosing a condition. That is, it is unclear as to what is intended to be the relationship between measuring the nucleic acid and obtaining the sample, detecting the HLA-G polymorphism and comparing the HLA-G polymorphism.


Art Unit: 1634

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (703) 308-2199. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)-308-1119. Papers related to this application may be faxed to Group 1634 via the PTO Fax Center using the fax number (703)-872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers
October 16, 2003


CARLA J. MYERS
PRIMARY EXAMINER